



Timo Nevalainen - COST B24: The Two Rs Initiative 2006

- Replacement is the ultimate objective
- It would be morally wrong not to extend the Two R alternatives to those animals still used
- The 7FP should include all the Three Rs in all areas where laboratory animals are used
- This was supported by 50 European Universities, research institutes and animal welfare organizations

The Two Rs dimensions

Refined
welfare

Less harm

Better
science?

More
animals

Fewer
animals

Poor
welfare

Any Two Rs method should

● be scientifically validated

Method

● be truly beneficial to the animals

Efficacy

● not detract from the scientific integrity

Safety

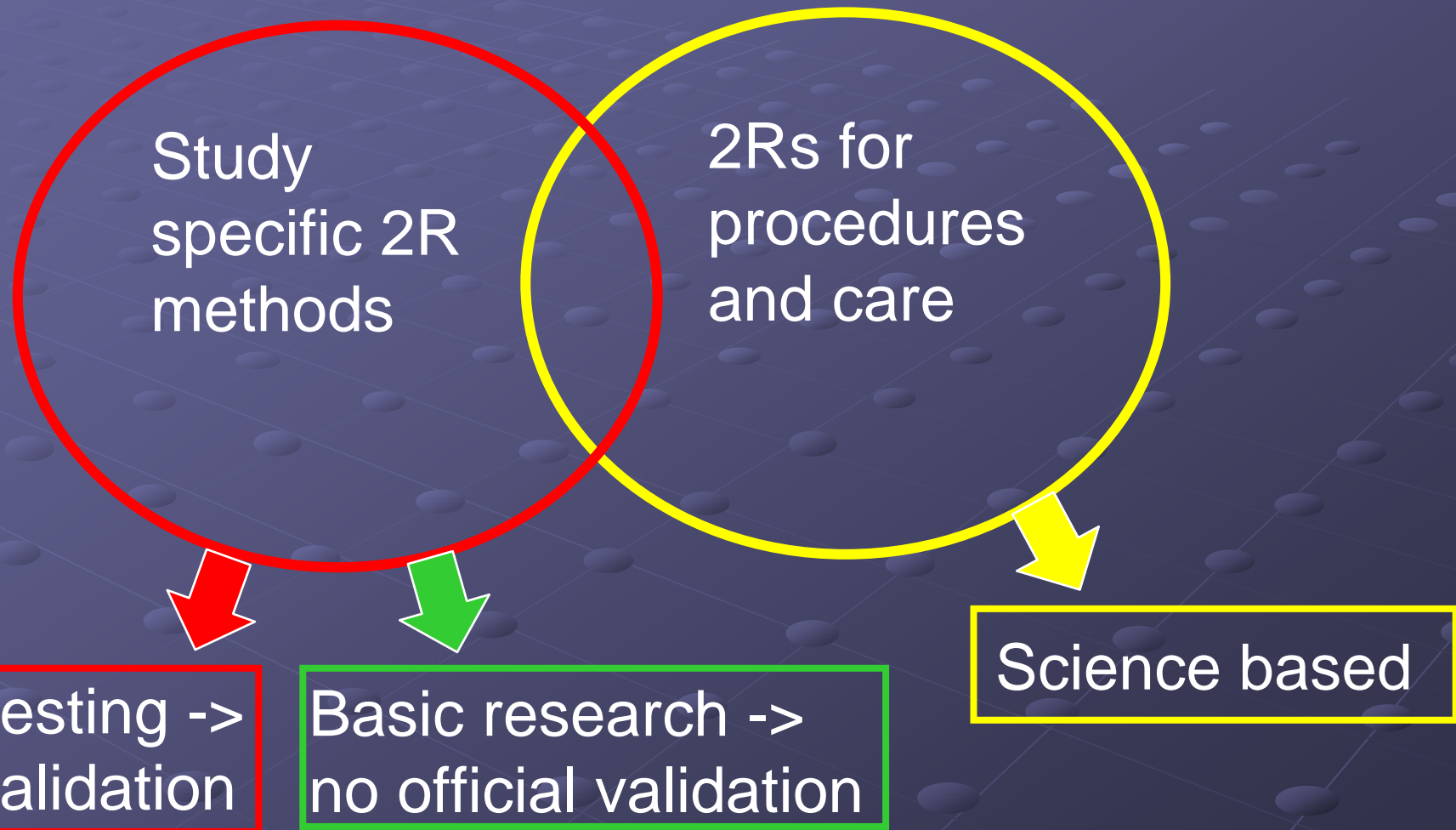
WHICH EVOLVES INTO BETTER SCIENCE?

The Directive

The Union Reference Laboratory

(a) coordinating and promoting the development and use of alternatives to procedures including in the areas of **basic and applied research and regulatory testing;**

The Two Rs & validation



Flab rats: Unfit animals are bad for experiments

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RATS and mice are the most widely used animals in biomedical research. They are hugely important in the early stages of drug testing, before clinical trials in humans can begin.

Unfortunately, laboratory rats and mice are not up to the job. They are kept under conditions that give them little opportunity for exercise, and at the same time they have access to as much food as they can eat. As a result they are overfed, unfit and obese.

Such "couch-potato" animals develop a range of health problems, including insulin resistance, diabetes, high blood pressure, impaired brain function, increased oxidative stress and inflammation. They also have elevated levels of glucose, triglycerides and "bad" cholesterol in their blood, and are more susceptible to cancer, neurodegenerative disease and kidney disease. Unsurprisingly, they die prematurely.

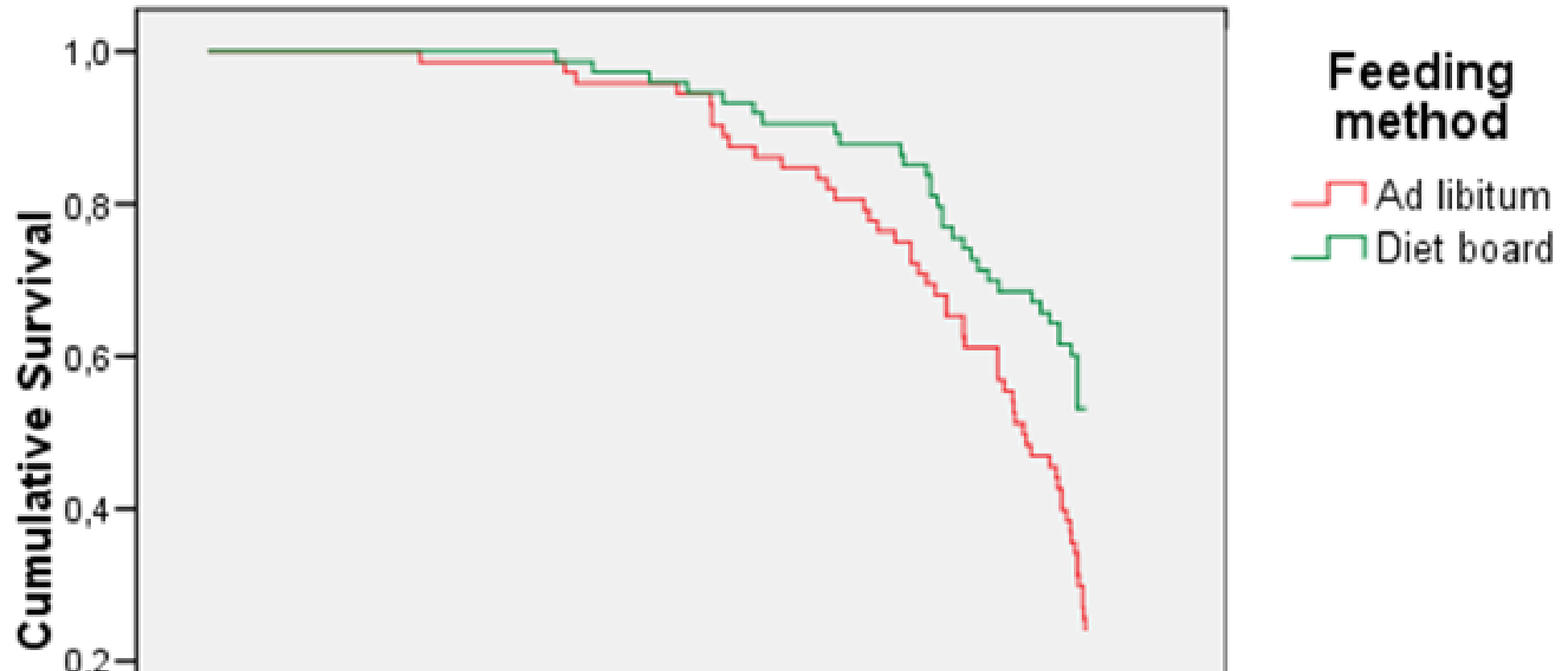
Obesity is especially problematic. Rodents kept under normal lab conditions gain weight throughout their adult lives. Up to 50 ...

Why do we then practice *ad libitum* feeding?

- Methods for restricted feeding
 - Labour intensive
 - Require single housing
 - Derail diurnal rhythms
- Less important in short term studies?



Kaplan-Meier survival curve (SPSS 15.0)



Survival status at the end of the study

	Females		Males		Total	
	<i>Ad libitum</i>	Diet board	<i>Ad libitum</i>	Diet board	<i>Ad libitum</i>	Diet board
Alive	4	13	13	25	17	38
Dead	32	23	23	14	55	37
Survival-%	11,1 %	36,1 %	36,1 %	64,1 %	23,6 %	50,7 %

The Challenges Ahead

- Use of animals continues
 - ERA / REACH / GAA
- Replacement not always possible for now
 - Animals should not be neglected
 - Huge potential for the Two Rs in both basic research and animal testing
 - Critical mass needed → EPAA's success
- FP7 should have funding opportunities for all 3Rs in all areas of animal based research